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Perspectives of Coronary Excimer Laser Angioplasty: Multiplexing, Saline Flushing, and Acoustic Ablation Control

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Background and Objective: **Bubble formation, pressure wave generation, and cavitations constitute major factors influencing the outcome of clinical Excimer laser angioplasty. Thus, the rationale of this study was to determine the extent of pressure waves occurring during excimer laser ablation and to discuss possibilities that allow a less traumatic plaque removal in the coronary circulation.**
Study Design/Materials and Methods: **Conventional and experimental Xenon-Chlorid-Excimer lasers emitting light at a wavelength of 308nm and a pulse duration of 115ns were used for testing of signals. Whereas the conventional excimer laser light source transmits light through all fibres of a 1.7 mm laser catheter simultaneously, the prototype excimer laser divides the laser beam into several areas of uniform energy fluence by scanning the beam from one section to the other using the intermission between two laser discharges. Hydrophones consisting of piezoelectric films detected the acoustic signals, which were obtained on normal arterial wall and atherosclerotic plaque.**
Results: **Multiplexing decreases maximum pressures for both normal arterial wall and calcified plaque significantly, whereas pressure rise time remains comparable. During ablation of pure blood, a linear increase of peak pressures of 1 MPa at 10 mJ/mm^2 to 7.5 MPa at 50 mJ/mm^2 is found. Contrast media intensifies the extent of pressure wave formation. At 20 mJ/mm^2, 60% contrast media added to blood results in an increase of maximum pressures from 1.5 MPa up to 5 MPa. Dilution with saline solution is effective; however, high concentrations of > 90% are required to achieve a significant pressure wave reduction.**
Conclusion: **Peak pressures of several thousand kPa occur during excimer laser ablation of contrast media, blood, calcified plaque, and normal arterial wall in a decreasing order. Multiplexing and saline flushing are capable of reducing the intensity of the generated acoustic signals during tissue ablation. It has to**

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be taken into consideration, however, that high concentrations of saline solution are necessary to achieve a significant reduction of peak pressures. Lasers Surg. Med. 21:72–78, 1997.

Key words: Excimer laser ablation; multiplexing; saline flushing; pressure waves

INTRODUCTION

Since 1988, approximately 15 thousand patients have been treated by eximer coronary laser angioplasty (ELCA). Recent publications underline the feasibility and safety of this technique [1,2]. However, all data also indicate that the incidence of restenosis following coronary excimer laser angioplasty is comparable to conventional percutaneous transluminal coronary angioplasty (PTCA). In addition, up to 80% of patients treated with ELCA require adjunctive PTCA, either due to an insufficient angiographic result or vessel complications such as vessel occlusion, major dissection, and perforation [3,4].

In view of these limitations, side effects of excimer laser ablation, such as bubble formation, pressure wave generation, and cavitations, have gained major interest and are subject to ongoing investigations [5,6]. Here, we provide a detailed description of the spatial and temporal distribution of pressure waves following excimer laser irradiation and discuss it with respect to practical considerations.

MATERIALS AND METHODS

Experimental Setup

In the experimental arrangement, Xenon-Chlorid-Excimer lasers (MAX 10 and MAX 20, Technolas, Munich, Germany) were used as the laser light sources. Both laser systems generate mean energies of up to 150 mJ at a wavelength of 308 nm and a pulse duration of 115 ns. The laser beam is transmitted through a circular aperture to select an area of uniform fluence and then focused by a lens into the waveguides. The pulse energy was measured by a photodiode joule meter and was varied from 2 mJ to 13 mJ, corresponding to energy densities of 15–50 mJ/mm^2.

The first laser system (MAX 10, Technolas, Munich, Germany) transmits the laser beam with a mean square area of 1.5 cm^2 into the catheter device, such illuminating all individual fibres within the catheter lumen (see Fig. 1). The second prototype excimer laser system (MAX 20 Fibre Scan TM, Technolas, Munich, Germany) reduces the laser beam area while maintaining an identical uniform energy fluence. Each such area is coupled into eight individual sectors of a specially constructed laser catheter device. Briefly, the focused laser beam is electronically aligned to each section of the catheter and scanned from one section to the other using the intermission between two laser discharges (see Fig. 2) [7]. Both technologies were tested using 1.7 mm laser catheters, consisting of 150 50-μm fibres, concentrically arranged around a central lumen for a 0.014″ guidewire.

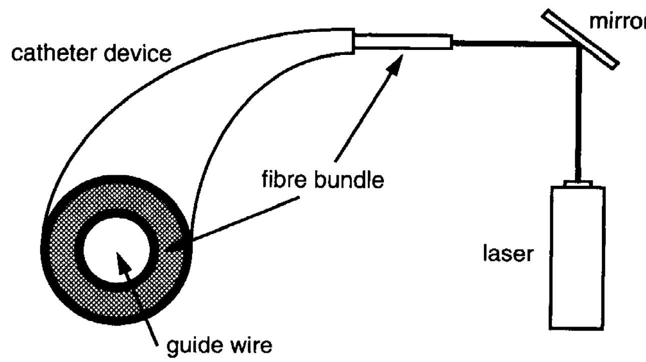

Fig. 1. Conventional excimer laser angioplasty: Simultaneous illumination of all fibres of the catheter device.

The acoustic experiments were conducted using tissue samples that were mounted onto a 50 mm^2 ×60 mm^2, 3-mm-thick lucite plate fastened to a metal support by spacers of 30 mm in length. The specimens were placed in a beaker filled with normal saline solution, blood, or contrast media. Since attenuation of ultraviolet laser pulses in normal saline solution is weak, the distance between the fibre tip and the tissue sample was set to the same order of magnitude as that of the hydrophone in order to avoid any perturbation of the acoustic signal. To account for the different hydrophone locations, the experimental results obtained in saline are normalized to a standard distance of 1mm, assuming an acoustic signal that is inversely proportional to the distance. If acoustic experiments were conducted in media containing blood or contrast material, all measurements were performed in a contact mode. It therefore

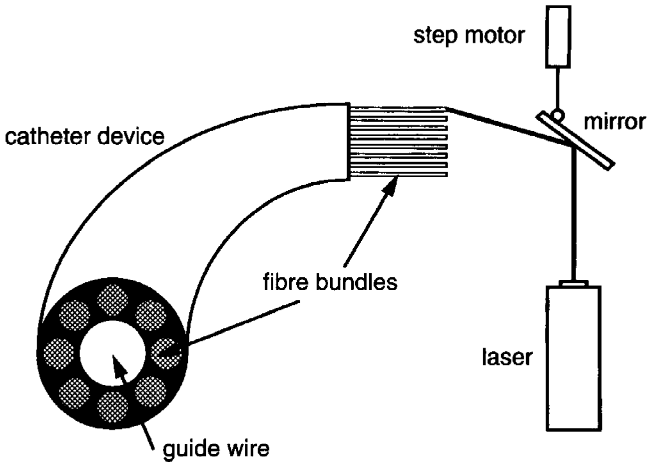

Fig. 2. Experimental excimer laser angioplasty: Multiplexing requires an electronic alignment of the laser beam to each section of the laser catheter device.

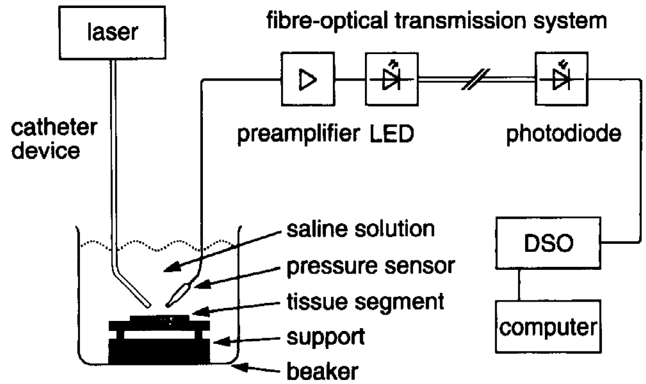

Fig. 3. Experimental arrangement for the detection of pressure pulses during excimer laser ablation.

has to be stated that differences in the pressure waveform characteristics may have been influenced by the mode of ablation, which is not taken into account in this report.

The acoustic signals generated by the laser pulses were measured with needle-type hydrophones that were developed at the Institut für Halbleitertechnik (Stuttgart University, Germany). The transducers had a responsitivity between 1.5V and 3.5V per bar and a frequency response of up to 20 MHz at least. The shortest rise time was 30 ns, despite the different thicknesses of the PVDF films of the individual hydrophones.

During the experiments, the hydrophones were placed 1–5 mm from the tissue samples. The distance was adjusted in order to obtain a sufficient signal when using a coaxial cable for signal transmission and to avoid saturation when using a fibre-optic transmission system. The acoustic signals were recorded on a dual channel digital oscilloscope (Philips PM 3323, Philips Gloeilampenfabricken, Eindhoven, The Netherlands), using either a 0.5 m coaxial cable RG 174 or a broadband fibre-optic transmission device that had been designed and produced at the Institut für Halbleitertechnik. The data were transferred to a personal computer for processing and storing. The oscilloscope was triggered by means of a fast (t-rise, t-fall 2 μs) Si-PIN-photodiode Siemens SFH 217 (Siemens, Munich, Germany) detecting the laser pulses transmitted by a second fibre (Fig. 3).

Tissue Material and Histologic Analysis

The acoustic experiments were conducted using sections of human aorta retrieved 24 hours postmortem. If necessary, they were frozen and stored at low temperature until use. Samples of 20 $mm^2 \times 20\ mm^2$ size with either calcified hard plaques or normal areas of arterial wall were identified in cooperation with a pathologist before testing for signals.

After the experiments, the tissue samples were stored in formalin, dehydrated, and buffered in paraffin. Staining was carried out using hematoxylin-eosin and elastica-van-Gieson stains.

Statistical Evaluation

All values are expressed as mean SD. The data were entered in the Statistical Analysis System (SAS Institute, Cary, NY). Statistical significance of differences in regard to maximum pressure, rise time, and pressure increase between normal and calcified arterial segments was determined using the two-tailed Student's test. Differences were considered significant at $P<0.05$.

RESULTS

A total of 888 acoustic signals were generated by the ablating catheter tip. All signals were analysed with respect to maximum pressure (MPa), rise time (ns), and pressure increase (kPa/ns) and were entered into the statistical analysis system.

Figure 4 depicts two typical pressure pulses, which are recorded 0.3–0.45 μs after the emission of the laser pulse. As opposed to ablation of normal arterial wall, the acoustic signal generated during irradiation of calcified plaque shows a higher peak pressure, a shorter rise time, and a higher pressure increase. Both signals have in common, however, the steep pressure increase,

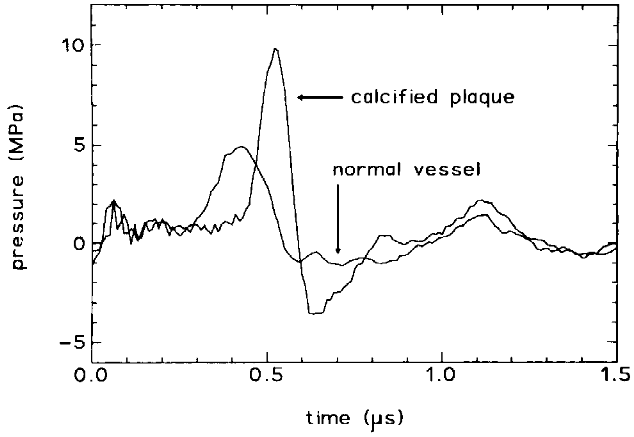

Fig. 4. Conventional excimer laser angioplasty: Two pressure pulses obtained during ablation of calcified plaque and normal arterial wall.

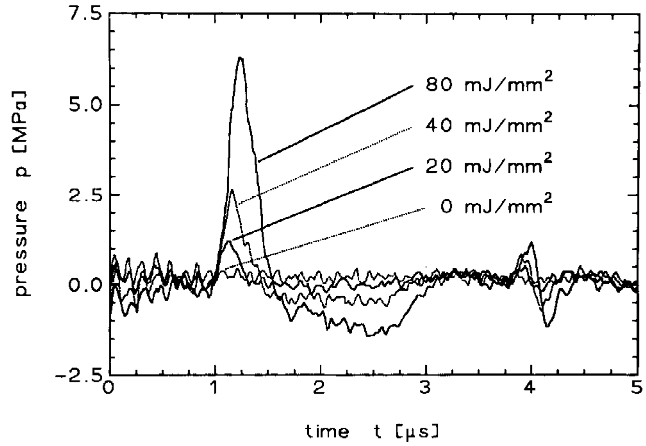

Fig. 5. Conventional excimer laser angioplasty: Influence of energy density on maximum pressures.

the fast deflection of the pressure curve, and a negative pressure following irradiation, the so-called cavitation.

By increasing energy density in a range of 20–80 mJ/mm^2, a proportional increase of maximum pressures can be found during ablation of calcified plaque (see Fig. 5). This increase of peak pressures ranges from 1 MPa at an energy density of 20 mJ/mm^2 up to 6.5 MPa at an energy density of 80 mJ/mm^2. This is remarkable, because an energy density of 20 mJ/mm^2 is considered to be too low for effective tissue ablation of severely calcified vessel segments (8).

While performing pressure wave experiments in pure blood, a linear increase of peak pressures is found, if the energy density is varied from 10 mJ/mm^2 to 60 mJ/mm^2. It must be noted that maximum pressures of 1 MPa are found at an energy density of 10 mJ/mm^2, which surpass 7.5 MPa at an energy density of 50 mJ/mm^2, if conventional excimer laser ablation is used (Fig. 6). Comparing conventional excimer laser ablation with multiplexing, a significant difference of peak pressures can be detected (see Fig. 6). This difference is also found for acoustic signals generated during ablation of normal arterial wall and calcified plaque in normal saline solution (see Figs. 7 and 8). It is obvious that this difference is more pronounced for signals detected on calcified plaque as compared to signals detected on normal arterial wall. It is also evident, however, that maximum pressures are up to threefold higher during ablation of pure blood as compared to ablation of atherosclerotic vessel wall segments.

Figure 9 depicts the effect of contrast media

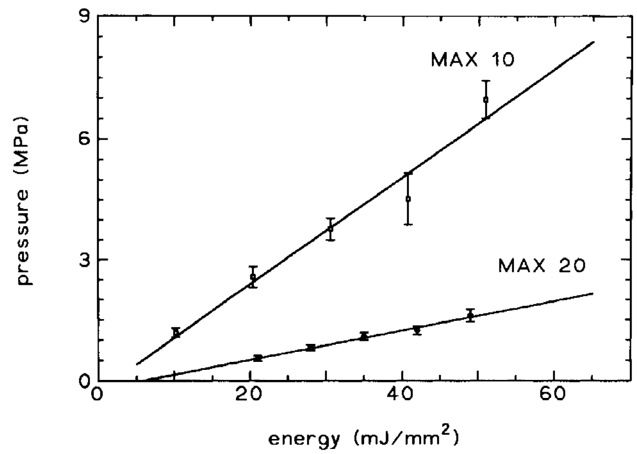

Fig. 6. Comparison of conventional (MAX 10) and experimental (MAX 20) excimer laser angioplasty during irradiation of blood.

diluted in blood, using a rather low energy density of 20 mJ/mm^2. With no contrast media diluted in blood, a peak pressure of 1.5 MPa is found, which increased twofold by the addition of only 20% of contrast media to the contrast media/blood solution. By increasing the concentration of contrast media, a further but less pronounced increase in peak pressure is found. Above a concentration of > 60% of contrast media diluted in blood, no additional increase of peak pressures can be detected.

The dilution of a blood medium with saline solution decreases pressure wave amplitudes as demonstrated in Figure 10. It should be taken into consideration, however, that concentrations

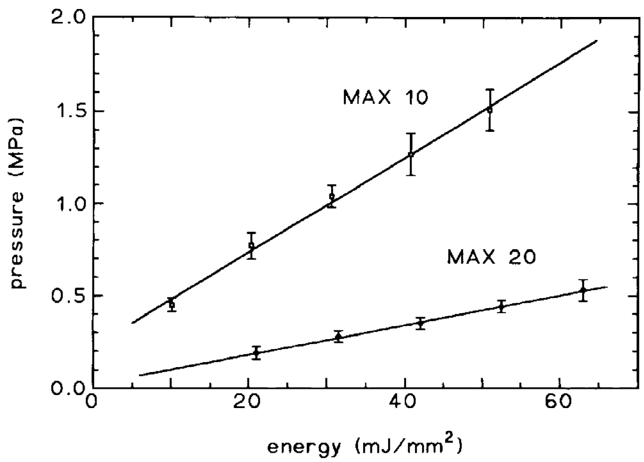

Fig. 7. Comparison of conventional (MAX 10) and experimental (MAX 20) excimer laser angioplasty during irradiation of normal arterial segments in a 0.9% saline solution.

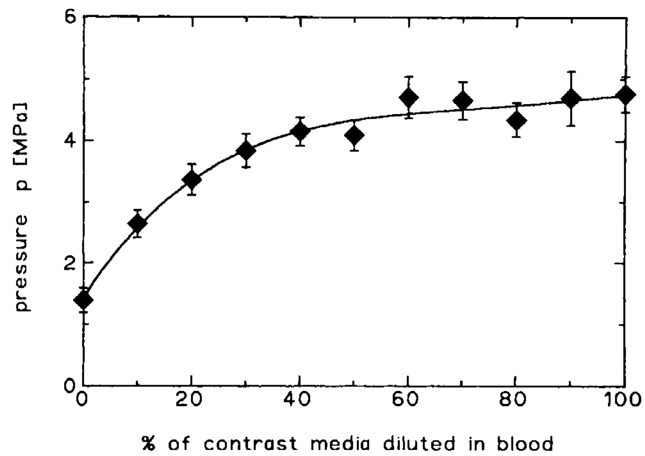

Fig. 9. Effect of contrast media diluted in blood with respect to peak pressure.

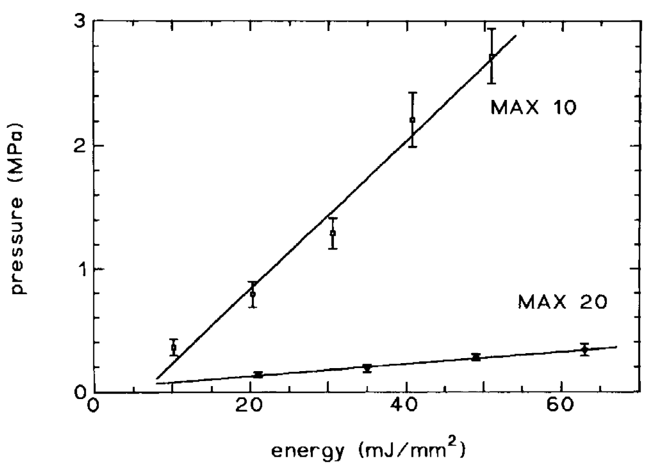

Fig. 8. Comparison of conventional (MAX 10) and experimental (MAX 20) excimer laser angioplasty during irradiation of calcified plaque in a 0.9% saline solution.

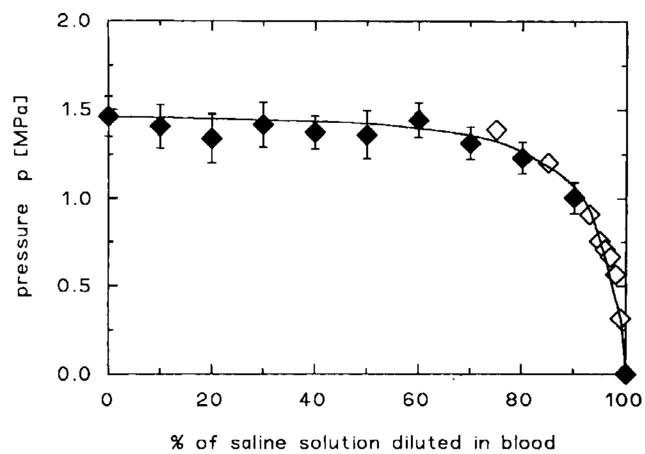

Fig. 10. Effect of saline solution diluted in a blood medium. High concentrations are required to achieve a marked reduction of peak pressures.

of > 90% are required to achieve a significant reduction of maximum pressures. Using a concentration of 95% of a normal saline solution diluted in blood, this reduction of pressure wave maxima is threefold at least.

Using a large pressure scale, it becomes evident that pressure wave recordings during ablation of normal arterial wall and calified plaque are strongly correlated with the applied pulse energy densities. Although the difference of the acoustic signals is strongly significant for both tissue types tested, both curves differ only little using this pressure scale. Stents, made of tantalum steel as in this case, display an extraordinary increase in maximum pressures. At high energy densities (40–60 mJ/mm^2), this difference is at least 20-fold as compared to the maximum pressures detected on calcified vessel segments.

Histological analysis of the 32 aorta segments used for these experiments validated the macroscopic classifiation of the two tissue types tested. It has to be taken into account, however, that the degree of atherosclerotic disease varied largely for all investigated arterial segments. It also has to be stated that the diagnosis of calcification was preferrably based on the macroscopic diagnosis rather than on histologic staining techniques.

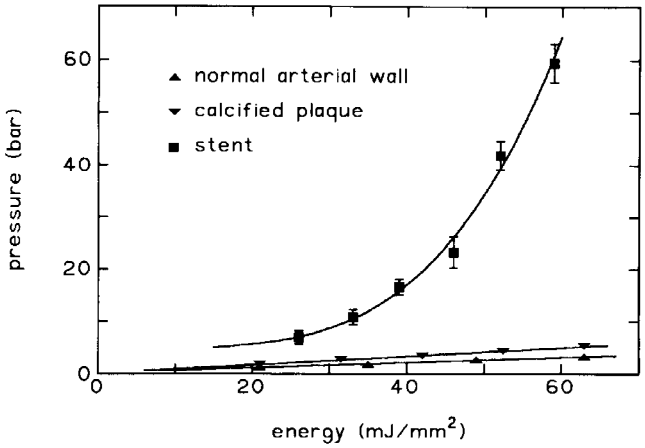

Fig. 11. Conventional excimer laser angioplasty: Comparison of the acoustic signals obtained during irradiation of normal arterial wall, calcified plaque, and stent material consisting of tantalum steel.

DISCUSSION

Pressure waves—rather than shockwaves—have been identified as secondary phenomena occuring during excimer laser tissue interaction [9]. As it has been shown in the results section, a good correlation of the magnitude of the generated pressure waves and the applied energy density can be found. Even at very low energy fluences, pressure waves can be detected. These pressure waves increase in a linear fashion with the applied energy densities in an energy range that was used for testing in this work. Energy densities of 50–60 mJ/mm^2 result in peak pressures of several hundred kPa, which are detected at a distance of 1–5 mm lateral to the ablating fibre tip. Assuming a signal that is inversely proportional to the distance pressure wave maxima of several thousand kPa may be expected in the center where ablation occurs.

Due to the absorption peaks of ultraviolet laser light in proteins and small molecules [10], pressure waves were also detected in blood and contrast media. Comparing the amplitude of the generated stress waves for blood and contrast media, significantly higher peak pressures are found for ablation of contrast material, probably due to their high content of salts. Dilution of blood and contrast media using normal saline solution does decrease the extent of pressure wave maxima. It has to be stated, however, that high water concentrations of > 90% to 95% are required in order to achieve a reduction of stress wave induction.

When ablating atherosclerotic plaque versus normal "elastic" arterial wall, significant differences with respect to maximum pressure, pressure increase, and rise time are found. This scattering of the experimental results is attributed to the heteroginicity of the investigated tissue samples. The different mechanical properties of hard calcified plaque and soft elastic arterial wall result in different acoustic impendancies. This leads to differences of the acoustic coupling of the irradiated vessel segment to the saline solution: hard plaque reflects most of the acoustic signal, whereas soft arterial wall allows easy propagation of the pressure wave front into the tissue as well as into the saline solution. Analysing the different characteristics of the pressure wave pulses, it should be stated that a more detailed discrimination of the varying degrees of atheroscerotic disease is currently not feasible. The large variety in the composition of atherosclerotic plaque does not allow a distinct attribution of an individual pressure pulse to a clearly defined part of tissue. More sophisticated experimental arrangements may facilitate a more detailed analysis of pressure pulses in vitro; it remains open to question, however, if acoustic ablation control also can be achieved by the analysis of stress waves in vivo.

Multiplexing does result in a significant reduction of peak pressures for all tissue types tested. The theoretical background for multiplexing goes back to the early 1980s and is based on the assumption that excimer laser ablation induces a mass explosion of the irradiated atherosclerotic target rather than cutting it slice by slice by molecular photodecomposition [11,12]. As we have shown, pressure waves do accompany each laser pulse below and above the ablation threshold. Above the ablation threshold, the intensity of the generated pressure waves is mainly influenced by three factors: energy density, ablation area of the catheter tip, and the mechanical properties of the irradiated tissue samples. Whereas energy density has to remain in a range of 30–50 mJ/mm^2, in order to guarantee effective ablation of noncalcified as well as calcified tissue [13], a decrease of the ablative fibre tip area will allow a reduction of the mass exploding per each individual shot. Ablation of less mass results in lower peak pressures and induces also smaller bubbles, as it has been shown elsewhere [14]. It has to be taken into consideration, however, that multiplexing is a highly sophosticated, fragile technique, which is also accompanied by the induction of a pressure wave front, which is then followed by a vapor bubble. Although multiplexing reduces the extent of these phenomena, the in-

creased repetition rate results in an eightfold higher number of applied laser pulses. As we have to realize the low ablation rate of 308 nm laser ablation [15], thousands of individual laser pulses will have to be applied to "remove the material" within a 1–2-cm-long lesion in the coronary circulation. Although not quantified, tissue fragmentation is to be considered as an inevitable part of excimer laser tissue interaction.

In the era of upcoming, effectively cutting laser tools, it remains open to question if multiplexing, saline flushing, or acoustic and fluroscopic ablation control will leave a "niche" for excimer lasers in coronary angioplasty [16].

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